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Research Article

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Interaction of Human Serum Albumin with Methotrexate: Stability and Structural Analysis

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Abstract

Human serum albumin (HSA) as the most abundant carrier protein in blood plasma has been widely studied. HSA is often used as a model to study of the drug and protein interaction. The interaction between Methotrexate with HSA has been studied by methods such as fluorescence. Thermodynamic parameters obtained from thermal and chemical denaturation of the Human serum albumin with and without the presence of Methotrexate was analyzed.

Tm values in melting point (Tm) of HSA in the absence of these compounds were calculated 320.9 K and in the presence of 50µM Methotrexate were obtained 318.4 K, 100µM Methotrexate were obtained 318.5 respectively .ΔG^{o} (298k) of HSA in the absence of Methotrexate were measured 41.14 kJ/mol and in the presence 50µM and 100µM Methotrexate were obtained 39.4 kJ/mol and 15.2 kJ/mol respectively.

Chemical denaturation of HSA carried out with urea and titrated amounts of the protein in 280 nm, ΔG^{o}(H2O) and Cm values were calculated in the presence of these compounds. ΔG^{o}(H2O) was calculated 13.43 kJ/mol in the absence of ligands, and 11.63 kJ/mol in the presence of 50µM Methotrexate and 11.1 kJ/mol for 100µM concentration of Methotrexate.

Cm value of the protein in the absence of the aforementioned compounds was 1.57 M and in the presence of Methotrexate 50µM and 100µM were 2.06M and 2.03M, respectively. Intrinsic fluorescence studies showed that Methotrexate decrease the intrinsic fluorescence intensity at 300-450 nm which consequently results in the instability of the protein structure of HSA.

Keywords: Human serum albumin, Methotrexate, Stability, Fluorescence, Denaturation.

Introduction

Human serum albumin represents important and the most abundant protein constituent of blood plasma and serving as a protein storage component. Recently, the three-dimensional structure of human serum albumin was determined through X-ray crystallographic measurements [1]. This globular protein consisting of a single polypeptide chain of 585 amino acids, which has many important physiological functions [2-3]. HSA considerably contributes to colloid osmotic blood pressure and realizes the transport and distribution of many molecules and metabolites such as fatty acids, amino acids, hormones, cations and anions, and many diverse drugs. It also makes possible to bind and carry through the bloodstream many drugs, which are poorly soluble in water [3]. It has been shown that the distribution, free concentration, and the metabolism of various drugs can be significantly altered as a result of their bindings to HSA [4].

Methotrexate a synthetic nonbiologic antimetabolite is first-line DMARD for treating RA and is used in 50-70% of patients.It is active in this condition at much lower doses than dose needed in cancer chemotherapy. Evidence supports its use in juvenile chronic arthritis and it has been used in psoriasis, PA, AS, polymyositis, dermatomyositis, Wegener,s granolomatosis, giant cell artritis, SLE and vasculitis and most used as chemotherapy.[5]